L4 ANSWER 38 OF 123 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:126790 BIOSIS
DOCUMENT NUMBER: PREV199698698925
TITLE: A DNA motif present in alpha-V integrin promoter exhibits dual **binding** preference to distinct transcription factors.
AUTHOR(S): Sharma, Harsh W.; Higgins-Sochaski, Kimberly; Perez, Jose R.; Narayanan, Ramaswamy (1)
CORPORATE SOURCE: (1) Oncol. Div., Roche Res. Cent., Hoffmann-La Roche Inc., 340 Kingsland St., Nutley, NJ 07110 USA
SOURCE: Anticancer Research, (1995) Vol. 15, No. 58, pp. 1857-1868.
ISSN: 0250-7005.

DOCUMENT TYPE: Article
LANGUAGE: English

AB Antisense inhibition of the RelA subunit but not the NFKB1 subunit of NF-kappa-B **transcription factor** results in a block of cellular adhesion and inhibition of tumor cell growth in vitro and in vivo. Studies aimed at dissecting the molecular mechanism of antisense relA action led to our identification of a kappa-B-like motif present in alpha-V integrin promoter. The alpha-V/kappa-B motif is closely related to RelA/c-Rel-**binding** sequences, such as 65-2 and TF-1. However, unlike these two kappa-B-like motifs, the alpha-V/kappa-B motif detected a nuclear Sp1 activity distinct from kappa-B activity which was subsequently confirmed to be derived from Sp1. In comparison to the conventional GC box-containing Sp1 motif, the alpha-V/kappa-B motif also binds in vitro to c-Rel and RelA but not to NFKB1. Antisense inhibition of RelA inhibited the alpha-V/kappa-B activity. Direct in vivo competition of alpha-V/kappa-B-**binding** activity by a **decoy** approach also resulted in inhibition of alpha-V/kappa-B activity in intact cells. A variant of the a alpha-V/kappa-B motif was found to retain the dual ability to detect Sp1 and the NF-kappa-B complex in the nuclear and cytoplasmic extracts. Such dual interacting ability of a DNA motif offers yet another way of gene regulation in vivo and hence can affect cellular growth. Our results identify alpha-V integrin as one of the molecular targets for rel A/NF-kappa-B and may explain growth inhibition by antisense relA.

L4 ANSWER 35 OF 123 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:18889 BIOSIS
DOCUMENT NUMBER: PREV199799318092
TITLE: Ets up-regulates MET transcription.
AUTHOR(S): Gambarotta, Giovanna; Boccaccio, Carla; Giordano, Silvia; Ando, Margherita; Stella, Maria Cristina; Comoglio, Paolo M. (1)
CORPORATE SOURCE: (1) Inst. Cancer Res., Univ. Torino Med. Sch., Strada Provinciale 142, Km 3.95, 10060 Candiolo, Torino Italy
SOURCE: Oncogene, (1996) Vol. 13, No. 9, pp. 1911-1917.
ISSN: 0950-9232.
DOCUMENT TYPE: Article
LANGUAGE: English

AB MET, a potentially harmful oncogene controlling invasive growth, is overexpressed in a significant percentage of human cancers. Since amplification of the MET gene occurs only in a fraction of these cases, we investigated the transcriptional mechanisms responsible for up-regulation of the promoter activity. The transcription driven by the 3.1 kbp DNA fragment containing the minimal promoter was studied by 5' progressive deletion analysis. The patterns of MET promoter activity suggest the presence of weak negative and positive elements in the region between 300 and 840 hp upstream to the transcription start site. The region encompassing the first 300 hp strongly upregulates the promoter. This region contains four putative **binding** sites for members of the Ets **transcription factor** family, known to be involved in invasive growth. Transient co-expression of Ets1 resulted in a strong enhancement of the MET promoter activity. Increased expression of the Met protein was observed in cells stably transfected with ETS1. Double stranded oligonucleotides with Ets consensus sequence were used as a '**decoy**' to inhibit **binding** to DNA native sites. They dramatically reduced the amount of Met protein in a human carcinoma cell line overexpressing the oncogene. Interestingly, Met activation induces transcription of ETS1 mRNA, showing that Ets proteins act both upstream and downstream to MET. These data indicate that members of the Ets family promote MET transcription and suggest their contribution to the invasive phenotype through overexpression of MET.